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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/341,505	07/12/99	JACKSON S	MEWE-005

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PAMELA SHERWOOD
BOZICEVIC FIELD & FRANCIS
200 Middlefield Road,
SUITE 200
Menlo Park CA 94025

EXAMINER	
ROBINSON, H	
ART UNIT	**PAPER NUMBER**
1653	12

DATE MAILED: 01/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/341,505	Applicant(s) Jackson et al.
	Examiner Hope Robinson	Group Art Unit 1653

☒ Responsive to communication(s) filed on *Nov 1, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-28* is/are pending in the application.

Of the above, claim(s) *7-18, 20, 21, 23, 24, and 26-28* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6, 19, 22, and 25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☒ received in Application No. (Series Code/Serial Number) *PCT/GB98/00095*.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4, 8*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-6, 19, 22 and 25) in Paper No. 11 is acknowledged. The traversal is on the ground(s) that the claims not be restricted because the inventions are not distinct and/or independent. Furthermore, the invention as claimed would not cause serious burden.

Applicant's arguments have been fully considered but are not persuasive because as stated in the prior office action the special technical feature of the claimed invention does not escape the prior art based on the reference cited of record (Wei et al.). In addition, the methods have different end points, process steps and because the process steps do not share the same special technical feature, unity of invention is lacking. Therefore, the claims are not so linked by a special technical feature under PCT Rule 13.2. Thus the lack of unity is maintained and is final.

2. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

Oath/Declaration

3. The Oath/Declaration is defective because it is missing the dates that the inventors signed it.

Specification

4. The specification is objected to because of the following informalities:

The specification is objected to because on page 1, line 4 (see also page 2, line 26) the English spelling of the word "characterization" appears (see characterisation). In addition, the word "ionizing" is spelled "ionising" on page 2, line 13 and the word "leukemia" is spelled "leukaemia". Note also that the specification is replete with the English spelling of other words such as "utilises, stabilise, recognising". Therefore, a word find process should be performed to remove the English spelling throughout the specification. See also page 13, line 22 where the word "interaction" is spelled as "interacion". Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-6, 19, 22 and 25 are rejected under 35 U.S.C. 112 first paragraph, because the specification while being enabling for DNA dependent protein kinase (DNA-PK), DNA ligase IV and XRCC4, does not reasonably provide enablement for the fragment, analogue, variant and derivative thereof. Page 1 of the specification asserts that the invention relates to methods of screening, peptides, mimetics and methods of use based on the discovery and characterization of an interaction between known proteins and that these interactions play a key role in DNA repair. The protein in question are XRCC4 and DNA ligase IV, further interaction between XRCC4 and DNA-PKcs/Ku. The specification does not provide sufficient information or guidance as to what type of interaction or the extent of the interaction/effect. For example, on page 4, the specification asserts that "the present inventors have shown that XRCC4 exists ... and demonstrated convincingly that it interacts with DNA ligase IV and also DNA-PKcs/Ku". Does the fact that XRCC4 interacts with the above protein give it a function? Further, the specification at page 6 indicates that the physiological function of mammalian ligase IV is unknown. In addition, the specification on page 7 asserts that XRCC4 was known to be involved somehow in Ku-associated DNA double stranded break repair (KADR) but its biological activity was obscure, thus the present invention established for the first time the biological activity of XRCC4, that is binding to DNA ligase IV. However, the mere binding activity does not disclose a specific

function for the protein XRCC4, especially since the specification discloses that a clear function for DNA ligase IV has not been flattened by science.

Although the specification asserts that the present invention has discovered that DNA ligase IV is important for double strand DNA break repair via non-homologous end joining (NHEJ). The specification does not provide any convincing evidence/data of the asserted function, nor any detail as to what the "strong interaction" between XRCC4 and DNA ligase IV involves nor what the "modulation of the interaction between XRCC4/DNA ligase IV and between XRCC4/DNA-PKcs/Ku entails (see pages 7-9).

Another embodiment of the present invention is to provide for modulating, interfering with or interrupting interaction between the XRCC4 and DNA ligase IV. What is the nature of this interaction or the effect of the interaction or mechanism of the interaction? The specification provides no guidance regarding the type of interaction. Furthermore, the specification on pages 15+ discloses that suitable fragments of XRCC4 or DNA ligase IV include those which include residues which interact with the counterpart protein. Further, smaller fragments, analogues and variants of this fragment may be similarly employed. Such peptide fragment are obtainable by means of deletion analysis and/or alanine scanning of the relevant protein making an appropriate mutation in sequence. Further, the specification provides a superficial discussion on derivatives, variants and analogues. Clearly, this description is lacking the size/type of fragment, and does not provide any features related to a derivative, variant or analogue commensurate in scope with the claims.

Furthermore, no substantive guidance/direction is given regarding the claimed assay method, how to find a test compound, how much XRCC4 is included, is modulation up or down, how is the interaction determined and no proper measuring steps are provided. See for example, on page 28, where the specification asserts that "precise format of an assay of the invention may be varied by those of skill in the art using routine skill and knowledge". An example is then provided of an "in vitro labeling study". However, this discussion is not limiting and does not breathe life into the claims, especially since the claimed invention is directed to "an assay method".

Absent exemplification of a specific assay to assay a specific compound the specification is not enabled for an "assay method" as claimed. Further, since no guidance or direction is provided regarding the test compound, the derivative, variant or analogue thereof, for DNA ligase IV, XRCC4 and DNA-PKcs/Ku it would require undue experimentation to be able to practice the claimed invention.

Thus, for all of the above reasons, the specification is not considered to be enabling without undue experimentation, because, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to enable one skilled in the art to be able to practice the invention commensurate in scope with these claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6, 19, 22 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 as written is confusing. It is recommended that the claim be rewritten with a numerical system that clearly identifies the method steps because items (a) and (b) is insufficient.

Claim 1 is indefinite because the claim recites "an assay method" and ends with "determining interaction" with no indication of how the claimed compounds are measured, thus is complete (see also claims 2-6). The claim is also indefinite because line 1 of the claim recites "a compound" and line 12 recites "a test compound", are these compounds the same? In addition, the claim recites "able to modulate and able to bind" which renders the claim indefinite because the use of the word "able" implies that there are times that binding or modulation will not occur. The words "able to" should be replaced with "which binds or modulates" (see also claims 2-4, 6, 19, 22 and 25). Claim 1 is further indefinite because the claim recites "interaction and interact". What is considered to be an "interaction" since binding or repelling can be considered as an "interaction". Note also that the recitation of the acronyms "XRCC4 and DNA-PK_{cs}/Ku" is insufficient to convey what the invention is without the spelled out meaning. In addition, the claim is indefinite because the word "including" is recited because there is no indication of how much of the substance or compound is included. It is also unclear what is meant by "modulate". Does

modulation mean inhibition or activation (see also claims 2 and 19). Furthermore, the claim is indefinite because the claim recites "and/or", and it is unclear as to whether the slash refers to "and/or" or just "or". The dependent claims are also included in this rejection.

Claim 2 is indefinite because the claim recites "derivative, variant, fragment or analogue thereof' without indicating what type, size or any particular feature these possess (see also claims 1, 5 and 6).

Claim 3 is indefinite because the claim recites "an assay method for a compound able to affect DNA ligase IV activity" and the claim does not provide any information as to what "affect" occurs, is it degradation or inhibition or decreased activity etc., (see also claims 4, 22 and 25)?

Claim 4 is vague and indefinite because it is not clear if "a protein having the amino acid sequence of SEQ ID No. 1" is the same protein according to Claim 1 (having transcription inhibitory activity).

Claim 5 is indefinite because the claim provides for the use of an assay method (to determine the activity of DNA ligase), but, since the claim does not set forth any steps involved in the method or process, it is unclear what method, process, or therapy the claim is intended to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Furthermore, the claim is indefinite for reciting "ability to join" because it is unclear if the word "join" refers to binding or annealing, etc. Also the use of the words "ability to" is indefinite because it is unclear when it is not "able to" perform that function.

Claim 6 is indefinite because the claim recites " suitable peptide fragments" and it is unclear what is considered to be "a suitable peptide". The claim is also indefinite for reciting the plural version of "phosphorylate"

Claim 19 is indefinite because the claim recites " a method which includes, following obtaining a compound" (see also claims 22 and 25).

Art of *Record*

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Zhiying et al. (Cell, vol. 83, no. 7, pages 1079-1089, December 29, 1995). Zhiying disclose the isolation of a human cDNA sequence, termed XRCC4, whose expression confers normal V(D)J recombination ability and significant restoration of DSBR(DNA-double strand break repair) activity to XR-1. Zhiying also disclose mutations of the gene which encode components of the DNA-dependent protein kinase (DNA-PK) complex (a serine/threonine kinase) comprised of the DNA end-binding subunits Ku70 and Ku80 that phosphorylates a number of in vitro targets including transcription factors and p53. DNA-Ku_{cs} activity is said to be dependent on its association with DNA-bound Ku.

Hartley et al. (Cell Vol. 82, pages 849-856, September 8, 1995). Hartley et al. disclose DNA-PK which is involved in DNA double-stranded break repair.

Conclusion

8. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday - Friday from 9:00 A.M. to 5:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600